



Fig. S1. *SPINK5* mutation identification and mRNA expression analysis. Direct sequencing of all *SPINK5* exons was used to detect mutations. Affected siblings are compound heterozygous for the c.1302+4A>T (intron 14) (panel a) and c.2240+1G>A (intron 23) (panel b) splice site variants, which are inherited from the mother and the father, respectively. Mutation c.1302+4A>T is in linkage with the known polymorphism c.1258G>A (p.Glu420Lys) on the maternal allele (pedigree, c). Both mutations affect *SPINK5* pre-mRNA splicing by activating exonic cryptic sites, the usage of which results in shorter transcripts with premature truncation (PTC) immediately downstream the D6 (c.1302+4A>T) (panel a) and D10 (c.2240+1G>A) (panel b) domains. Full-length transcripts carrying the c.1258G>A polymorphism (indicated by the asterisk in panel a), thus in linkage with mutation c.1302+4A>T, are also detected.